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St. Bartholomew's Hospital Journal,

DECEMBER, 1902.

"Æquam memento rebus in arduis
Servare mentem."—*Horace*, Book ii, Ode iii.

Mr. Butlin.

MOST of our readers are already aware that Mr. Butlin has retired from active work in the Hospital.

Although too young to be affected by the superannuation rule, and still full of energy, he has decided that he can no longer carry out the duties of Surgeon to the Hospital and at the same time continue his private practice. Every one regrets that he should have been obliged to come to this decision, and he himself must have been very loth to give up work in which he took so much interest.

It was in the year 1868 that Mr. Butlin obtained his first official appointment in this Hospital. The house surgeon of Mr. Paget (not yet Sir James) resigned at a time when his appointment had still six months to run. Mr. Butlin replaced him, and not only finished the appointment, but also did the work for two months for his successor.

The following year he commenced to practise in the country, but the life was not congenial to him, so he gave it up and returned to London in 1870.

He next became attached to the Hospital for Sick Children in Great Ormond Street as registrar. This appointment was not obtained without a severe fight. But that will occasion no surprise when it is remembered that the unsuccessful candidate was Mr. Malcolm Morris.

Not very long afterwards Mr. Butlin was appointed assistant surgeon to the West London Hospital.

His hope was still to come back to St. Bartholomew's, and this wish was gratified when in 1872 he was made surgical registrar.

At the present time it would seem that the next natural step would be on to the permanent staff of the Hospital; but that was not the case in 1872.

The status of the surgical registrar at that time was not as high as it is now. It was not considered equal to that of the senior demonstrator of anatomy. The post was, in fact, usually held by a man who also had some other appointment which gave him a superior claim as candidate for the staff.

Some idea of the general opinion about the registrarship may be gathered from a remark of Mr. Butlin's predecessor: "The post is of no use, and no one will ever get on to the staff through it."

The great value of the post as conferring on its holder the opportunity for clinical observation was evidently not recognised, whilst the prophetic part of the statement was

proved untrue when Mr. Butlin was appointed assistant surgeon in 1881.

He had been registrar for over six years, and after that demonstrator of practical surgery.

Within a year of his appointment as assistant surgeon he took charge of the throat department. He soon became deeply interested in this work, and, as is his invariable custom, succeeded in making the subject interesting to others. An increasing number of students attended the department, which was transferred to the surgery. Still later, as the increased importance of the work done there was recognised, the number of days on which patients attended was increased to two in the week instead of one.

In 1892 Mr. Morrant Baker retired from the surgical staff, and Mr. Butlin became a full surgeon. This position he has filled for ten years, and now amidst universal regret feels compelled to resign.

In this brief record of his association with the Hospital we have made no attempt at an appreciation of Mr. Butlin as a surgeon, for he is still in the full tide of surgical practice; nor is this the place in which to give an account of his connection with the various societies of which he has been president and treasurer. But it may not be altogether out of place to refer briefly to the loss which the Medical School is sustaining by his retirement.

Mr. Butlin has always delighted in clinical teaching. To go over a case with his class and dressers, to make them observe its essential features, and so arrive at a diagnosis, was always a source of keen pleasure to him. His method of teaching was always fresh and clear. He asked pertinent questions and expected straightforward answers. He had no compunction in exposing any one who tried to hedge, and attempts to elude him in this way were singularly unsuccessful. He acted up to his own precepts in this respect, and always had the courage to commit himself to a diagnosis. It is not surprising, therefore, that his classes were well attended, and that it was well known amongst those working for the final Fellowship examination that his Monday afternoon class was something which should not be missed.

The Specific Antibodies.

By W. D'ESTE EMERY, M.D., B.Sc.(Lond.),
Assistant Bacteriologist to the Royal Colleges of Physicians and Surgeons.

(*Read at the Abernethian Society, December 4th*, 1902.)

THE subject of my paper to-night is one which originated out of the study of immunity, although it is one which has no necessary connection therewith, nor even with the subject of athology. Let me, however, briefly outline to you the views generally held concerning immunity and the process of recovery from infections in the year 1890. At that date the chemical theories of Pasteur and Chauveau had long been ancient history, and the theory of phagocytosis was energetically and ably supported by Metchnikoff and the majority of the French school of pathologists against the humoral theory of Buchner and others; while an intermediate position was held by Hankin and other supporters of the cellulo-humoral theory. Metchnikoff held leucocytes to be the main if not the only means for the protection of the body against bacterial invasion; that they had the power of engulfing and digesting living and virulent bacteria, and that their success or failure in the conflict determined the recovery or death of the patient. The upholders of the humoral school, on the other hand, attributed the destruction of the bacteria to the action of substances which are dissolved in the fluids of the body, and to which Buchner gave the name of *alexins*. The researches into the nature of these alexins, which were published between 1887 and 1894, were numerous, but nothing very definite was proved by them. The only point which seemed to be fairly well established was that they were very unstable substances which could easily be destroyed by heat and chemical materials, and which soon disappeared when the serum was kept. The upholders of the cellulo-humoral theory maintained that these substances emanated chiefly or entirely from the leucocytes, and explained the collection of leucocytes which occurs in an inflamed area as being a contrivance for increasing the supply of the bactericidal substance at the region at which it was most required. It is scarcely necessary for me to remind this meeting of the brilliant researches in which our lamented master, Professor Kanthack, demonstrated that in some cases, at any rate, these protective substances occurred in the leucocytes in the form of eosinophile granules.

At this period the fact that bacteria bring about the symptoms of disease by means of their poisons or toxins was clearly recognised, and a great deal of investigation into the chemical nature of these toxins had taken place. Here again the results were unsatisfactory, the only certain fact proved being that they were of proteid constitution, though, except in a few cases in which they had been proved to be albumoses, the exact group of proteids to which they belonged was uncertain.

I have said that it was clearly recognised that the symptoms of bacterial diseases were due to the action of the toxins on the cells of the host. In spite of this comparatively little importance was attached to the question of immunity to toxins. In support of this statement I may point out that all the theories of immunity which had been promulgated before the year 1890 attempted to explain the removal or destruction of the bacteria, and passed over the toleration of toxins which is displayed by immune animals as of little importance, or as insusceptible of explanation. But in 1890 there appeared two papers from Behring's laboratory dealing with tetanus and diphtheria, which entirely changed the trend of thought among pathologists, and which laid the foundation for the most remarkable discoveries in pathology and physiology which have been made since then. To sum up their results, they proved that the serum of animals which had been strongly immunised or "hyper-vaccinated" against tetanus or diphtheria by injection of cultures of the appropriate bacilli or of their toxins would act protectively when injected into a second animal together with the living culture; that this serum also possessed curative properties, checking the course of an experimental infection if injected at a period not too late after inoculation; and lastly, that it possessed the very remarkable power of neutralising the soluble poison produced by the bacilli, so that a small quantity of serum from an animal vaccinated against diphtheria would save the life of a second animal inoculated with an amount of diphtheria toxin many times larger than would be sufficient to cause death if no serum were injected at the same time or shortly after.

The first thing to notice about these sera is that they are—to use a word which is very convenient, though scarcely susceptible of exact definition—they are *specific*. An animal which is inoculated with tetanus yields a serum which is potent against tetanus toxin, but which has no power against that of diphtheria, and *vice versâ*. The sera of animals inoculated against these two diseases contained the first examples of specific antibodies to be discovered, and these were soon followed by the production of antibodies to abrin and ricin, proteid poisons of vegetable origin, and snake-venom, also a proteid poison.

So far I have refrained from giving these substances the names by which they are so familiar to you. The term *antitoxin* was not used until some time later, when the method of its action had been fairly well proved. At this early date several theories were held. Metchnikoff, for instance, argued that it acted as a stimulant of the phagocytes. The theory which was more generally accepted, and

which may now be considered as proved, is to the effect that antitoxin is a definite chemical substance which forms a definite chemical compound with toxin, this compound being devoid of poisonous properties. Briefly, the chief arguments in favour of the chemical theory were—(1) the combination takes place according to the law of multiple proportions, although in some cases, as in that of diphtheria, the relation is very complicated; (2) the process takes place more rapidly at a high than at a low temperature; (3) diphtheria toxin will pass through a film of gelatine on a Chamberland filter, whereas its antitoxin does not. Now if a mixture of these in neutralising proportions be passed through such a filter the toxicity of the filtrate is abolished or greatly reduced. It is suggested that if the two did not combine unaltered toxin would come through. The theory of cytic stimulation was supported by experiments of Calmette on snake-venom, which is resistent to heat, whereas its antitoxin is easily destroyed. Now a mixture of the two in neutralising proportions regains its toxicity when heated, and it was supposed that if the two had combined this could not occur. But Martin and Cherry showed that the combination takes place slowly, and that the mixture does not regain its activity if kept for some time at the temperature of the body before being heated. Perhaps none of the proofs is entirely satisfactory, but taking them altogether we may consider the chemical theory as fully proved, and the term antitoxin as justified.

The discovery of the antitoxins against tetanus and diphtheria changed the aim of researches on immunity. The study of phagocytosis and of the bactericidal power of the blood was abandoned for a time in favour of attempts to prepare bacterial toxins and procure antitoxins for them. In the majority of cases these attempts were doomed to failure. The sera of animals which had been vaccinated against other organisms were found to be protective, but not antitoxic. For example, a small quantity of cholera serum would protect an animal against infection with cholera, but was found to contain no substance which would counteract the little-known cholera toxin. Cholera serum differs from diphtheria serum in that the latter alone is antitoxic, though both are protective.

In 1894 Pfeiffer made a statement which threw a certain amount of light on this phenomenon. He showed that the peritoneal fluid of an animal vaccinated against cholera has the power, whilst still in the body, of destroying the cholera vibrio. He injected a quantity of cholera culture into the peritoneum of a vaccinated guinea-pig, and withdrew a small portion after a few minutes. The organisms had become deformed and granular. In a few minutes more they were transformed into small coccus-like masses, and in a little while had entirely disappeared. This was an absolutely new phenomenon. The previous investigations of the humoral and cellulo-humoral schools had dealt with the death of the bacteria, not their digestion and solution. The latter had been tacitly assumed to be brought about by intra-cellular processes in phagocytes. Many pathologists confirmed Pfeiffer's discovery, and extended its application to the typhoid bacillus and many other organisms; this reaction also was found to be specific. Further, some argued that if the peritoneal fluid could dissolve the vibrios *in vivo* it should be able to do so *in vitro*, and tried the experiment. The results differed; in some cases the organisms were dissolved, in others they were unaltered. Metchnikoff, who was gradually being driven from the position he held with regard to phagocytosis, and forced to acknowledge that bacteria might at least be injured extra-cellularly, was the first to explain the discrepancies by showing that Pfeiffer's reaction can always be obtained *in vitro* if the peritoneal exudate or blood-serum from the immunised animal is perfectly fresh. Now Pfeiffer had shown that his reaction might be obtained if, instead of an immunised guinea-pig, a normal one were used, provided that a small amount of cholera serum were injected into the peritoneum with the culture. The solution of the mystery was suggested by Bordet, who proved that two substances are necessary for the reaction: firstly, a substance which for the present I shall call the antibody to the organism, and which occurs in the serum of the immunised animal; and secondly, a substance which occurs in the serum of all animals, immunised or normal. The latter is readily destroyed by heat and disappears on keeping, and is what I have previously spoken of as *alexin*. Bordet's explanation was that the former substance acted on the bacteria in such a way as to render them sensitive to the action of the alexin, and he called it the sensitising substance. Bordet showed that both substances—the sensitising substance and alexin—are present side by side in the fresh serum from an immunised animal, and that the antibody resists heat, while the alexin is readily destroyed. He also showed that the reaction can be obtained with immune serum which has been rendered inactive by heat, provided a quantity of normal and perfectly fresh serum from the same species of animal be added. Bordet's discoveries were of the highest importance, although his explanations are not generally accepted at the present time. Into this, however, I do not propose to enter. I wish simply to refer to the discovery of the second group of antibodies—those concerned in the extra-cellular digestion of bacteria in the bodies of highly immunised animals. Like the antitoxins, they are specific; the antibody to cholera has no effect on the typhoid bacillus.

Bordet also showed that antibodies to another and entirely different group of cells can be obtained in a similar manner. Buchner had already discovered that the fresh serum of some normal animals has the power of dissolving the red blood-corpuscles from another species; for example, the serum of a rabbit will dissolve the red corpuscles of a guinea-pig, and eel's serum rapidly dissolves the corpuscles of most or all mammalia. This power is destroyed by heat. In 1898 Bordet discovered that a similar phenomenon is manifested by serum from an animal which has been injected with the blood-corpuscles from another species. Thus a normal rabbit's serum is without effect on the red corpuscles of a fowl, but if we inject the rabbit with fowl's corpuscles its serum will acquire the power of dissolving these corpuscles. This hæmolysis is exactly like bacteriolysis, as seen in Pfeiffer's reaction. Two substances are necessary, a specific antibody which is formed as a result of the injection of the corpuscles to be destroyed, and a highly unstable substance which exists in normal blood. This discovery was the germ of many and important researches, and it was soon followed by the preparation of antibodies against leucocytes, ciliated epithelial cells, nerve-cells, spermatozoa, kidney cells, etc., and it was realised that the mechanism by which the bacterial invaders are destroyed in the living body is also applicable to the removal of all sorts of cells of foreign origin. We may call this group of specific antibodies the cytolysins or cytotoxins; they are substances which are formed as a result of the injection of foreign cells into a living animal; they are not destroyed by moderate heat, and they have the power of dissolving the cells in question when they are assisted by an appropriate alexin.

In following up the development of our knowledge of bacteriolysis and hæmolysis we have passed over the discovery of another group of specific antibodies—the *agglutinins*. These were first discovered about the year 1896 by Gruber and others, though certain isolated examples had been noted before this. For instance, in 1889 Charrin and Roger saw that cultures of *B. pyocyaneus* in the serum from an immunised animal were different from cultures in broth or serum from a normal animal. They described the former as being clear and transparent, the bacilli being united in little clots at the bottom of the tube. Metchnikoff had described a similar clumping, as early as 1891, as occurring when serum of an animal immunised against *V. Metchnikovi* was added to a culture of that organism, and was even prepared to look upon it as a general reaction, but failed to find it with one of the organisms with which he worked. Gruber showed that the serum of an animal which had been injected with a culture of the typhoid bacillus possessed the power of paralysing that organism, and of causing it to collect in clumps, but had no power over other bacteria, and suggested the reaction as a means of identifying the typhoid bacillus. Widal, in the same year, used the reaction in the reverse way as a test for typhoid fever. It was soon found that the reaction is given by most pathogenic organisms, and also by other cells. For example, if we take the serum of a rabbit which has been injected with fowl's corpuscles, heat it so as to destroy its alexin, and thus take away its hæmolytic properties, and then add it to a suspension of fowl's corpuscles, we shall find that the latter are clumped just as the typhoid bacilli are in Widal's reaction. In a similar way we can prepare agglutinins for leucocytes, epithelial cells, etc. The agglutinins are not the same as the cytolysins, although they usually accompany them, and were at first thought to be identical.

The last group of specific antibodies are the *precipitins*. The first record of them that I have been able to find was in the year 1899, when Tchistovitch showed that animals could be immunised to eel's serum, a powerfully poisonous substance, and that the serum of animals so immunised would give a precipitate when mixed with eel serum. This was soon shown to hold for other sera; if, for instance, we inject a goat with horse's serum we find that after a time the goat's serum will give a precipitate when mixed with horse's serum. This reaction has been proposed as a test to determine the species of animal from which a given sample of blood was taken; for example, it was thought that an antihuman serum might be prepared by injecting animals with human serum,

and that it would give a precipitate with human serum, and remain clear when mixed with serum from one of the lower animals. So far the results are not very satisfactory, for the serum of an animal which has been injected with that of another species will give precipitate not only with that, but also with serum from many other species. This need not surprise us when we consider how complex a fluid serum is, and what an innumerable variety of proteids it contains. But Myers went a long way towards proving that the reaction is truly specific by showing that the serum of an animal injected with a solution of a proteid as pure as could be obtained gave a precipitate with solutions of that proteid, but not with any other.

Thus these specific antibodies fall into four great groups:—(1) The *antitoxins*, which have the power of combining with and neutralising toxins. With these are included some other substances (antialexins, antienzymes, etc.) which have similar properties. (2) The *agglutinins*, which have the power of clumping the cells by the injection of which they are formed in the living body. (3) The *precipitins*, which unite with the proteids which lead to their production, and form insoluble compounds with them. (4) The *cytolysins*, which, in presence of a suitable alexin, have the power of dissolving or digesting cells. There are also more complicated anti-antibodies, such as anticytolysins, which I shall not discuss.

The whole range of biology hardly presents a single phenomenon as remarkable as that which we see in the production of antibodies. A poison, when injected into a living animal, has the power of producing its own antidote—an antidote, be it observed, which is powerless against other poisons; and cells injected into a living animal lead to the production of a substance which causes the digestion of that variety of cell, and of it alone. The production of antibodies is of enormous theoretical interest as well as of great practical importance. There is but one theory which accounts in a satisfactory way for the observed facts; this is Ehrlich's side-chain theory, which it is my main purpose to develop to you.

In the first place I must point out that although we speak of these antibodies as being specific, and as being called forth by the injection of the substances mentioned, they do occur in normal blood. For instance, diphtheria antitoxin is quite common in the serum of normal horses: sometimes as much as 4 units are present per c.c. Agglutinins also are common in normal blood. Human blood will clump a suitable culture of anthrax bacilli, often in high dilutions, and horse's serum clumps typhoid bacilli, *B. pyocyaneus*, and, less powerfully, the cholera vibrio. Hæmolysins were first discovered in normal sera. Rabbit's serum, for example, will dissolve guinea-pig's corpuscles. I am not aware whether precipitins have ever been found in normal blood, or whether they have ever been looked for. So general is the presence of antibodies in normal blood as to justify us in restating the problem, and in asking, not how are these antibodies *formed* by the injection of the causative substances, but how are they *increased* by this process? We shall see the importance of this later.

Secondly, it is important to notice that all the substances to which we can procure antibodies are *proteids*. In the case of most of the toxins our knowledge of their nature is only indirect. We know that they are destroyed by heat and by digestion, and that they are precipitated by the precipitants of proteids. In the case of the precipitins, cellulysins, and agglutinins our knowledge is more direct. Proteids, and proteids alone, have the power of leading to the formation of antibodies. Now there are no definite chemical characters by which we can recognise proteids; they all contain certain elements in approximately constant proportions, and are either able to supply food-nitrogen to the living body, or are closely allied in their chemical constitution to substances which have that power. In other words, our fundamental conception of a substance which has the power of inducing living bodies to produce antibodies is that it is a food substance.

Now let me make a long digression, and recapitulate in outline our knowledge of the constitution of diphtheria toxin. When the great therapeutic value of antitoxin was realised the necessity for some method of estimating its strength and of standardising it was soon felt. But the dosage of antitoxin is quite unlike that of other drugs, for it has no effect on the healthy body, and only affects any toxin which may be in the system. The volume, weight, or physiological action on healthy animals, the means by which other drugs are measured, do not help us here, and we can only tell the strength of a sample of diphtheria antitoxin by finding the amount of a given toxin which a given bulk will render inert. This is a simple matter as long as we want merely relative results. If we keep a sample of toxin we can easily find how much antitoxin it takes to neutralise a certain amount,—for example, 1 c.c. But such results depend entirely upon the strength of the test toxin, and would not enable us to compare antitoxin from one laboratory with that from another where a different test toxin was used. In the search for an absolute standard several units were tried and abandoned, and at last it was decided to consider as the unit of toxin the smallest amount which is certainly fatal in four days to a guinea-pig weighing 250 grammes. Guinea-pigs differ very little amongst themselves in their susceptibility to diphtheria toxin, and are the most suitable animals to use as the indicator in the process of titration. And it was decided to define the unit of antitoxin as the amount which exactly neutralises a hundred of these minimal lethal doses of toxin. Now I must remind you that the diphtheria toxin never has been and probably never will be isolated in a pure form, and I must draw a distinction between the toxin, by which I mean the product of the diphtheria bacillus which kills an animal in a short time, and the diphtheria poison, by which I mean the broth in which the bacilli have grown, the bacilli themselves having been removed by filtration. I will now give you an example of the method by which the constitution of diphtheria poison has been determined, and I shall follow Ehrlich's earlier system rather than his most recent one, as being simpler and sufficiently accurate for the purpose in hand.

The first thing to be determined is the minimal lethal dose of the sample of diphtheria poison in question by injection of varying amounts into test guinea-pigs. We will suppose it to be ·01 c.c., that is, that a hundredth of a c.c. of the poison will kill in four days a guinea-pig weighing 250 grammes. Then by our definition 1 unit of antitoxin will completely neutralise 1 c.c. of this poison. If we inject a mixture of 1 unit of antitoxin with 1 c.c. of the poison into an animal no effect whatever will be produced. This amount of poison is what Ehrlich calls the Lo dose. For this poison, therefore—

$$\text{Lo} = 1{\cdot}00 \text{ c.c.}$$

Now let us add to this neutral mixture one lethal dose of the poison. We should expect that the guinea-pig into which we inject the whole would die in four days, for we have added a whole lethal dose more than the antitoxin will neutralise. But it does not die; it recovers, though there may be local œdema, and, after a time, paralysis. Further experiments show us that we must add much more than one lethal dose if the animal is to be killed in four days; the exact amount can be determined, and is called the L+ dose. Let us suppose that it is 2·01 c.c. Thus for the poison in question we must add twice as much poison as the antitoxin can neutralise before a single lethal dose is left over. Ehrlich's explanation (which is undoubtedly the correct one) is, that there are several substances present in the poison, and that they all combine with antitoxin, though with different degrees of avidity, and that they differ greatly in their poisonous power. To go further with our analysis let us take the Lo dose, *i.e.* 100 lethal doses, and add to it $\frac{199}{200}$ of a unit of antitoxin. We should not expect this dose to be fatal, as one half a lethal dose is uncombined, and it is not. Now let us take the Lo dose and add to it $\frac{198}{200}$ of a unit of antitoxin; here we should expect $\frac{1}{100}$ of the 100 lethal doses to remain free and the animal to die, but again it does not, though it may suffer from œdema and paralysis. We go on in this way reducing the amount of antitoxin until we have added only $\frac{150}{200}$ of a unit, and still the mixture does not kill. But when we add only $\frac{149}{200}$ of a unit of antitoxin a single lethal dose is set free, and the animal dies in four days. We go on reducing the amount of antitoxin, and now we find that for every $\frac{1}{200}$ of a unit less we leave unneutralised enough toxin to kill a guinea-pig in four days. Thus if we mix the Lo dose of our poison with $\frac{148}{200}$ of a unit, and divide the mixture into two halves, each will kill. One c.c. of poison *plus* $\frac{147}{200}$ antitoxin will kill three guinea-pigs, and so on until we come to a mixture of 1 c.c. poison *plus* $\frac{50}{200}$ of a unit of antitoxin, which will kill 100 pigs. But if we reduce the amount of antitoxin still further no more toxin is set free, and no more than 100 pigs will be killed. In other words, we may take 100 lethal doses of poison, and add to it a quarter of a unit of antitoxin without diminishing its lethal action in the least, and the whole lethal power of the whole 100 doses is taken away when we have added one half of a unit more. Thus it appears that the first and last quarters of the unit of antitoxin are wasted in combining with some substance which does not kill the guinea-pig. These results Ehrlich represents by the following diagram, which he calls the spectrum of toxin (Fig. 1, upper part).

The space represents the Lo dose, that is the amount which is neutralised by one unit of antitoxin. It is divided into 200 parts, and the substances which occur in the poison and have a strong

affinity for antitoxin are placed at the left-hand side of the diagram, whilst those which have less are placed at the left. It shows that as we reduce the amount of antitoxin no toxin is left free until only $\frac{149}{200}$ of a unit has been added, after which each reduction of $\frac{1}{200}$ of a

FIG. 1.

unit sets free one lethal dose until the whole hundred have been released. The explanation of this is that the poison contains a substance which has a greater affinity for antitoxin than toxin has, but which is devoid of lethal action. It is called *prototoxoid*, and has to be saturated before the toxin can take up any antitoxin. You remember that in estimating chlorides by titration with silver nitrate you add a little chromate of potash to the solution to be tested. The silver has a greater affinity for the chloride than for the chromate, and you get a white precipitate of silver chloride until all the soluble chlorides have been decomposed, and then you begin to get a chocolate-coloured precipitate of silver chromate. In precisely the same way when you add antitoxin to diphtheria poison the first portion added goes to combine with the prototoxoids, and these must be completely saturated before any toxin is neutralised. When all the toxin has been exactly neutralised a substance still remains which has the power of producing œdema and paralysis. This is called *toxone:* it combines with antitoxin, but with less avidity than toxin and with far less avidity than prototoxoid, and is less poisonous than toxin, though more poisonous than prototoxoid, which is quite inert.

Now let us keep this sample of toxin for some time. We shall find that it has undergone a change, becoming much less toxic, but that it has not lost any of its power of combining with antitoxin. To take a particular case, we may find that the toxic power has fallen to one half, so that the minimal lethal dose is now one fiftieth, instead of one hundredth, of one c.c. Yet the Lo dose is unaltered: a unit of antitoxin will still neutralise exactly 1 c.c. of the poison. The spectrum is now represented in the lower part of Fig. 1. In this case if we add only $\frac{150}{200}$ of a unit of antitoxin to the Lo dose only the toxone will remain unneutralised as before. But if we add $\frac{149}{200}$ only half a lethal dose of toxin will remain over, instead of a whole dose, as was the case when we first examined the sample. In other words, half of the toxin has undergone a change, being converted into a substance which Ehrlich calls *toxoid*, which has exactly the same affinity for antitoxin that toxin has, but which is entirely devoid of lethal power.

Now we recognise toxin by two properties: firstly, its power of producing poisonous symptoms; and secondly, its power of combining with antitoxin. These experiments teach us that these properties are resident in two different portions of the toxin molecule. A molecule of toxin must be considered as being composed of a *haptophore* group, which has the power of uniting with antitoxin, but which has no lethal power; and of a *toxophore* group, on which the lethal activity of the whole molecule depends (see Fig. 2, where A is a toxin molecule, B its toxophore, and C its haptophore groups). The latter resembles the alexins in that it is readily destroyed, and when it has been destroyed toxoid is left. A molecule of toxin which has lost its toxophore and retained its haptophore group is a molecule of toxoid: it retains its power of combining with antitoxin, but has lost all its poisonous properties (Fig. 2, D). We can form no idea of a toxophore group which has lost its haptophore group, and such a molecule is not known to occur. Toxones must be regarded as possessing a haptophore group similar to that of toxin, but having a lesser affinity, and a toxophore group of less potency. Prototoxoid also contains a haptophore group, and one which has an intense affinity for antitoxin, but no toxophore group.

I have said that we recognise toxin by its two properties—the power of injuring living animals, and its power of combining with antitoxin. The latter we see to be due to the union of a haptophore group with a corresponding group of the antitoxin molecule. Now the production of poisonous symptoms is due to the formation of a compound between the toxin and the protoplasm of the cells the vitality of which is injured. Is there any reason for thinking that the poisonous action of the toxin is due to a combination between the toxin and the cells of a nature similar to that which takes place between the molecule of toxin and the molecule of antitoxin? There is. This was proved by Wassermann in the case of tetanus, and has since been extended to other toxins. We know that tetanus acts chiefly on the central nervous system: now if we take an emulsion of the brain and mix it with tetanus toxin in suitable proportions we find that the latter loses its power, and is no longer virulent when injected into animals. In other words, the brain substance contains a group of atoms exactly similar to the group in tetanus antitoxin which combines with the haptophore group of the tetanus toxin. These observations are of great importance: we have seen that antibodies occur in normal serum, and now we find that they occur in normal cells, and, even more important, that they occur in the very cells which are affected by the toxin in question. We may fairly deduce from this, firstly, that the *antitoxin originates from the cells that the toxin attacks;* and secondly, that *a cell is attacked by a given toxin because it contains a group of atoms with which the haptophore group of the toxin unites.*

At first sight it would appear that the possession of such groups would be a great disadvantage to the cell, inasmuch as it would permit of its being injured by the toxin. But when we consider the fact that all the toxins for which we can get antitoxins are proteids we begin to see some explanation of the anomaly. A cell must be nourished, and it obtains its nourishment from the proteids which occur in the fluids with which it is bathed. These proteids must be attracted from the fluid before they can be built up into the protoplasm of the cell. Now Ehrlich has formulated the idea that a cell (or rather a living molecule of cell protoplasm) consists physiologically of two portions. There is a portion which is a sort of executive centre, and discharges the functions of the cell; and there is a less highly organised portion, the function of which is to nourish the cell itself. This is supposed to be more peripheral, impinging on the fluid with which the cell is bathed, and to consist of what are called *side-chains* (Fig. 2, E, E). The term is borrowed from organic chemistry, where it is used to denote the radicles attached to a benzene nucleus, etc. These side-chains (or receptors, as they are often called) have the function of uniting with the haptophore groups of the food proteids which are present in the lymph and blood. The molecule thus united to the cell undergoes a process akin to digestion, is built up into the protoplasm, and is used for the nutrition of the executive centre.

When the proteid which is present in the blood is poisonous the first stage of the process takes place just as in the normal nutrition of the cell; the haptophore group of the toxin finds a side-chain which it fits, and unites with it. But the possession of the toxophore group confers poisonous properties on the toxin, possibly by acting as a sort of enzyme, and submitting the cell to a process of digestion. The side-chain which has united with the haptophore has discharged its duty in seizing nourishment, but the captured molecule has proved too strong for the captor. *Intoxication with proteid toxins is physiologically a process of nutrition* (Fig. 2, where a toxin molecule is shown united to a side-chain).*

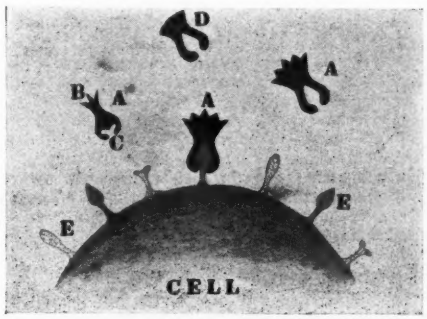


FIG. 2.

Now let us suppose that a few only of the side-chains are grappled by the poisonous molecules, and that the cell becomes ill, but is not fatally injured. The side-chains are necessary for the nutrition of the

* In this and the following figures molecules of toxin and other primary proteids are rendered in black, whilst antibodies and side-chains are grey.

cell, and the latter reacts like a lowly organism,—for instance, like a hydra when some of its tentacles are cut off. The useless side-chains are restored, fresh ones being formed; this is shown in Fig. 3.

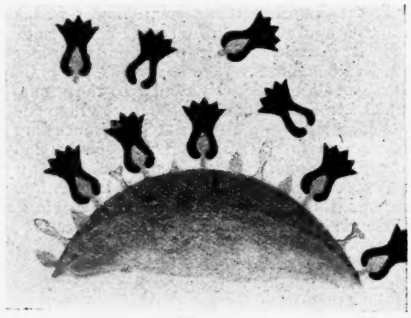


FIG. 3.

Suppose now that these fresh side-chains are attacked by a fresh dose of toxin; they, too, will be rendered useless, and must be restored. If we regulate our dose nicely these fresh ones may in their turn be rendered useless and again replaced. In this way the cell is stimulated more and more powerfully, and the production of fresh side-chains goes on more and more rapidly. In fact, the cell is gradually being trained to produce these side-chains, and the more practice the cell gets the more rapidly it is able to do so, and at last it acquires the habit, if I may put it in that way, of forming these side-chains on small provocation. If we still increase the stimulation without bringing about the death of the cell we may cause a phenomenon similar to that which is seen in processes such as inflammation, where the reaction takes place out of proportion to the strength of the stimulus. This process may go to such an extent that the side-chains become more numerous than the cell can carry, and become cast off into the surrounding fluid (Fig. 4). Now these side-chains contain a group

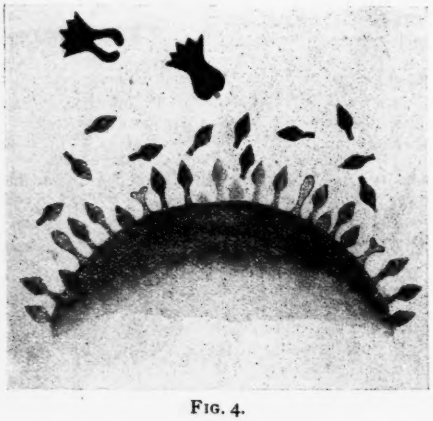


FIG. 4.

of atoms which exactly fits the haptophore molecule of the toxin by which the cell has been stimulated to produce them. They constitute antitoxin; and *the side-chain which by uniting the toxin to the cell permitted it to exercise its lethal action is now free in the blood, and by uniting with the toxin before it can reach the tissues prevents it from doing any damage.* Out of the nettle danger the cell has plucked the flower safely. This is Ehrlich's explanation of the production of antitoxin, and it explains the process without introducing any but well-known laws and phenomena.

We can easily see why only proteid poisons call forth the production of antitoxins. The union of a poisonous proteid with the side-chain of a cell is quite different from the combination of a poison like nitrate of silver with the living protoplasm. The first process may be compared to the insertion of a key which fits the lock, and is a process akin to that which is constantly taking place in all cells. The latter resembles rather the violent smashing of the lock, and is a process for which no preparation has been made in nature. Ehrlich supposes that the union of the proteid molecule is firmer than that of the non-proteid poison. I am doubtful whether this is correct, but it is quite certain that the poisoning of a cell by these non-proteid poisons is of a nature entirely different from nutrition. The cell is affected as a whole, and no especial side-chains are picked out to be regenerated by the still living cell.

On this theory, if we inject a solution of a proteid into a living animal four events are possible.

Firstly, the proteid may be one which occurs normally in the blood of the animal. In this case it unites with the cells, haptophore to side-chain, and is absorbed into the living protoplasm of the cell. In this case no antibody is produced. This is the process by which the cell is nourished, and the injection of the proteid simply makes the blood a little more nourishing.

In the second case the proteid may be poisonous,—that is to say, it may contain a toxophore group. In this case, if its haptophore group finds a suitable side-chain the two unite, and the first process of nutrition occurs. But the toxophore can now exert its deleterious effect, and the cell is poisoned. In this case, if the poison is exhibited in suitable doses an antibody (antitoxin) is formed.

Here let me point out that the term poisonous is a relative one,—relative, that is, to the animal injected. Eel's serum is not poisonous to eels; its proteids are built up into the living cells, and no antibody is formed. But if we inject eel serum into rabbits it acts as a toxin, and an antitoxin is formed.

Thirdly, the proteid may be non-poisonous, but it may be useless for the nutrition of the cells of the animal injected. It unites with its appropriate side-chain, but the process goes no farther. This is the process which takes place in the production of precipitins. The side-chain to which the proteid is attached is rendered useless and has to be regenerated, and under suitable circumstances is regenerated in excess and cast off, and this although the cells have never been ill.

Lastly, it is possible that the proteid may find no side-chains which its haptophore will fit. In this case it will be useless as nourishment, and will produce neither toxic symptoms nor antibody, but will probably be eliminated in the secretions. The actual existence of this possibility is difficult of proof, but it may account for some of the cases of immunity to toxins.

Let me now briefly pass in review one or two points connected with the different groups of antibodies.

The antitoxins have been dealt with already, and require but little further consideration. But it is well to notice that Ehrlich's theory enables us to explain why antitoxin is formed in quantity far greater than would neutralise the toxin which is injected into the animal. The cells have been stimulated to produce side-chains in quantity out of proportion to the stimulus. They are, so to speak, in a state of hypersensitiveness, in which a slight stimulation calls forth a great reaction. It also explains why the production of antitoxin goes on so long after we cease injecting antitoxin: the cells have acquired fresh habits, which are not lightly lost. Lastly, it explains the phenomenon which I believe to be very important in practical medicine—the loss of immunity to one disease in the presence of a second infection. Cells that have been trained to cast off one set of side-chains, to produce one variety of immunity, lose this power if we train them to cast off a second and different set. This phenomenon is capable of proof in the laboratory, and is illustrated every day in medical practice.

The production of the precipitins depends upon a process akin to the formation of antitoxin, but differing from it in that the cell is submitted to no danger: there is no immediate risk to the cell if the side-chain remains some time united to the haptophore of the foreign proteid. In other words, the stimulation is not so powerful and the antibody is produced in smaller proportions.

But why should precipitin, *plus* its causative proteid, result in the formation of an insoluble molecule? A mixture of toxin and antitoxin gives no precipitate. It possibly depends on the size of the molecule. The bacterial toxins are mostly peptones and albumoses, and these, as we know from experiments in dialysis, have small molecules. A molecule of antitoxin probably consists of a molecule of ordinary coagulable proteid, usually globulin, modified by the addition of a specific side-chain. The addition of the small molecule of toxin to this has but little effect. But we may assume that the effect of the union of one giant molecule of coagulable proteid with another results in the formation of a molecule so large that it cannot remain in solution. It is probable, however, that the phenomenon is more complicated than this, and that the process is really one of clumping, the giant proteid molecules being clumped like the bacilli in Widal's reaction.

The theory also enables us to explain the fact that precipitins are not formed, or are formed only in small amounts, if we inject an animal with serum from another animal closely allied to it zoologically. At the same time the serum of two animals even of the same species is somewhat different, and I have thought that I have found minute traces of a substance which would precipitate with horse serum in the serum of horses which had been injected with large quantities of horse serum.

We must regard the agglutinins as antibodies to the *non-poisonous* proteids in the bodies of the bacteria which we inject, and as closely allied to the precipitins. The exact mechanism of the formation of clumps has yet to be settled. There are five or six theories, but by far the most plausible is that of Bordet, who holds that it is due to a change in molecular relations between the bacterial or other cells and the fluid in which they float. That is, it is caused by a change in surface tension. I may remind you of the fact that if two bodies, of which one is wetted and the other is not wetted, float on the surface of a liquid, they tend to repel one another, whereas if neither or both of them are wetted they tend to approach one another—in other words, to clump. Similar processes take place in the depth of fluids, as when particles of oil in emulsions run together to form drops. It is easy to imagine that the surface tension between the water and the molecules of proteid in the bacilli or other cells is altered by the union of molecules of agglutinin with the latter, and that they tend to approach one another.

There is, however, an alternative solution which requires a moment's consideration. Kraus has shown that the substance which unites with agglutinin, and which is present in the body of the bacilli in young cultures, passes out into the broth in old cultures; and that if we take an old culture of typhoid bacilli (filtered to remove the bacteria) and add to it some typhoid serum, we get a precipitate. Here we have a phenomenon exactly like that presented by the precipitins: there is a proteid present in the bacilli, and injection into an animal gives us a substance which precipitates the original proteid. Paltauf suggested that a similar phenomenon takes place when bacilli clump. Some of the proteid is present in the fluid, and when its precipitin is added a coagulum is formed which contracts, enmeshes the bacilli, and in contracting draws them together in clumps. It is a fact that if you take an old filtered culture of typhoid bacilli, and add to it small particles of any sort—an emulsion of clay, some staphylococci, etc.—and then some typhoid serum, you get typical clumping just as you do in Widal's reaction.

We conclude of agglutination, therefore, that the exact mechanism of the process is uncertain, but that it is due to the combination of the proteid present in the body of the bacilli or in the surrounding fluid with its specific antibody.

The fundamental unity of agglutinin and precipitin is shown by the fact that the peculiar property of each is destroyed by a temperature of 60° C. If you heat an agglutinating serum to 60° C. it will no longer clump, but Kraus showed that serum thus treated still possesses the power of combining with the bacterial proteid, and heated precipitin has the power of combining with its appropriate sero-proteid, though it does not precipitate it. Thus we are justified in believing that the molecules of agglutinin and precipitin consist functionally of two atom groups,—a thermo-stable haptophore group, which unites with the proteids from the bacteria or serum; and a thermo-labile group, on which the peculiar clumping power depends. When the latter is destroyed the former is left, and the substance can then combine, but not clump; such a substance is called *precipitoid* (Fig. 5, C). Since this is the case for agglutinin and for precipitin, it is clear that the two are identical. Agglutinin clumps bacteria or other cells, and precipitin clumps giant molecules of proteid. We may call them bacterio-precipitin and sero-precipitin respectively.

These substances are formed from receptors of a more complicated nature than those which give rise to antitoxin, for the latter consist functionally of a single haptophore group, whereas the precipitins consist of a haptophore and a peculiar functionating group on which the clumping properties depend. This is shown in Fig. 5, in which the complex side-chain is shown at B in Group II. In this figure A represents the primary proteid (toxin, giant molecule of coagulable proteid, etc.), B the side-chain, C the antibody, and D the neutral compound.

I can deal but briefly with the most interesting group of the antibodies, the cytolysins. I have already shown how an animal can be immunised to any sort of cell, and that the serum of such an animal possesses the power of dissolving that cell. Let us consider the hæmolysins, for they have been studied most. A rabbit's serum will not dissolve ox corpuscles, but acquires the power of doing so if we inject the rabbit with defibrinated ox blood. If we heat the serum of the immunised rabbit the power is lost, but it is restored by the addition of some fresh serum from a normal rabbit. This, of course, is exactly similar to Pfeiffer's reaction.

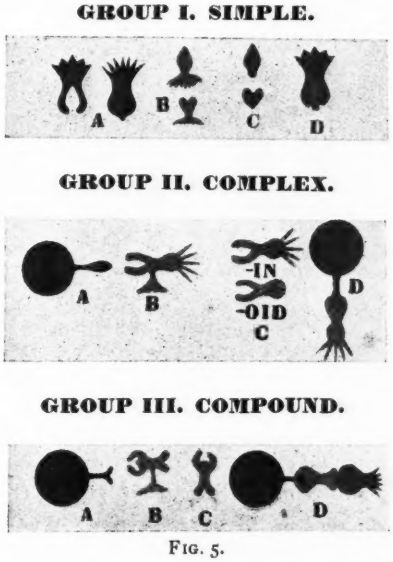


FIG. 5.

Many explanations have been put forward as to the mechanism of this solution. Ehrlich's, which is now generally though not universally accepted, is that the injection of the corpuscles causes the production of an antibody which has a haptophore group, which can combine with the side-chain of the red cell injected. This antibody is called amboceptor, desmon, intermediate body, immune body, *substance sensibilitrice*, etc. etc. The term most generally used is amboceptor, but desmon is somewhat more convenient. It is a stable substance, and is not readily destroyed by heat. It has the power of combining with the red cells, haptophore to side-chain, and can do so at a low temperature, but the red cell is quite unaltered in appearance when saturated with desmon.

For the solution of the cells a third substance is necessary, and this is present in normal serum. It is called alexin, addiment, complement, etc., and is soon destroyed by a temperature of 55° C. or by keeping. It has no power of injuring an ordinary red cell, but it can combine with desmon which has combined with a cell, and when it does so the cell is dissolved (see Fig. 5, III, D, showing a compound of a proteid molecule, desmon, and alexin). This solution only takes place at the temperature of the body.

The following experiment exhibits in a simple form the chief properties of these substances. Fresh serum from an immune animal (for example, from a rabbit which has been injected with ox corpuscles) is mixed with ox corpuscles and the mixture kept at a low temperature for a few hours. Under these circumstances no solution takes place. It is supposed that the desmon has united with the corpuscles, but that the alexin has not united with the desmon.

This experiment and the proposed explanation of the result are shown diagrammatically in Fig. 6, where A represents the ox corpuscles, and B and C the fresh immune serum, B being the alexin and C the desmon. The truth of the explanation is proved thus:—The mixture is centrifugalised and the supernatant fluid (Fig. 6, D) separated from the deposit of corpuscles (E), and each is tested separately.

To the deposit (Fig. 7, E) of red corpuscles some fresh normal serum (rabbit serum) is added. This contains alexin (F). The mixture is kept at 37° C., and solution of the corpuscles soon takes place. Clearly, therefore, the corpuscles have undergone some change which renders them vulnerable to the alexin of normal serum. This change consists in their union with desmon; the alexin can now attach itself to the desmon, and thus indirectly to the cell (G). All the conditions for hæmolysis are now present.

Now let us turn to the supernatant fluid (D in Fig. 6 and Fig. 8). This, we assume, contains alexin which has not been able to attach

itself to the desmon at the low temperature. If we add to it some normal ox corpuscles (H) and keep the mixture at 37° C. no hæmolysis will take place. This might possibly be due to deficiency of alexin. Let us therefore add some fresh normal serum; still there is no hæmolysis. This can only be due to lack of desmon, since the other necessary substances, alexin and corpuscles, are present. To

FIG. 6.

prove that this is the case we add some heated immune serum (containing desmon, but no alexin, as shown in J), when complete hæmolysis takes place (Fig. 8, K). The same result would have occurred had we added heated immune serum without previous addition of fresh normal serum.

Thus we have proved that desmon unites with the red corpuscle

FIG. 7.

in the cold and with alexin at 37° C., and that the two together are able to dissolve the red cell. Desmon, therefore, has *two* haptophore groups, one for the cell it attacks and one for alexin; hence its name of amboceptor. It is formed from a receptor which is even more complex than those which give rise to precipitin (Fig. 5, III, B). It is suggested that the function of these double-haptophored receptors is the assimilation of giant proteid molecules by means of alexin, which acts as a sort of digestive enzyme. Thus when a cell has to nourish itself with a giant proteid molecule it first seizes this with one haptophore of a double-headed receptor, and seizes an alexin molecule with the other; the alexin is then supposed to be able to digest the molecule, and the cell to absorb the products of decomposition.

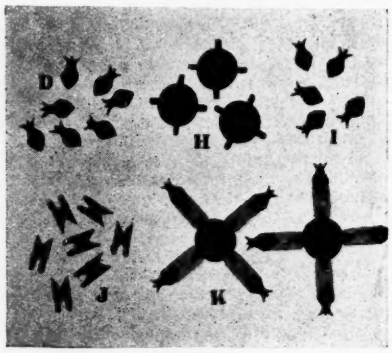


FIG. 8.

As far as we know at present, most of the facts which have been worked out for hæmolysins are true for bacteriolysins and the other cytolysins, and it is assumed that the mechanism I have attempted to explain is of great importance in the removal of the bacteria from the body in the recovery from infectious disease and in immunity. In this respect the chief interest attaches to alexin. I think it is now fairly certain that alexin originates mainly or entirely from the polynuclear leucocytes. This is a fact of great importance, for it explains the reason for the collections of leucocytes in an inflamed area, and affords a basis for a compromise between the supporters of the cellulo-humoral theory, the phagocytotists, and the modern school which attributes immunity to the presence of antibodies.

The nature of these alexins is perhaps the most interesting and pressing question of the day. They are enzyme-like bodies with a haptophore which is relatively stable, and a zymophore or toxophore group which is easily destroyed by heat. In this they are analogous to toxins, and just as toxins are converted into toxoids, so are alexins converted into alexinoids. They are not antibodies; they occur in normal serum, and might fitly be called animal toxins. We can prepare antialexins to them in precisely the same way as we prepare antitoxins.

The chief questions concerning them are—will the alexin which dissolves one cell, *e.g.* an anthrax bacillus, dissolve another species, *e.g.* a staphylococcus? Will the alexin from one species of animal functionate with the desmon from another? The practical importance of this is very great. For instance, the bacteriolytic sera, such as antityphoid serum, contain desmon, but the alexin accompanying it disappears long before it is used, and they are usually derived from a horse. The practical value of these sera depends on whether the serum of the patient possesses alexin which will activate the horse desmon; and the future progress of sero-therapy appears to depend on the discovery of an animal which has alexin with a haptophore group exactly resembling that of the alexin of man.

A Case of Pneumonia with Distended Gall-bladder simulating Acute Abdominal Disease.

By C. HAMILTON WHITEFORD, M.R.C.S., L.R.C.P.

THE patient, a tall stout man of seventy-one, had been under my care at the Plymouth Public Dispensary on several occasions for rheumatism and chronic bronchitis. On December 14th, 1899, he came to me complaining of pain and tenderness in the right hypochondrium, having as usual a cough. I ordered him fomentations and sent him home to bed. During the night he had pain in the region of the umbilicus,

shooting up into the right side of the abdomen. The pain was severe, made him vomit, and kept him awake. His bowels acted last on the 14th; the motion was stated to have been dark. An enema given on the 15th produced no result. There was no jaundice. At midday on the 15th the abdominal condition was as follows:

The abdomen moved slightly on respiration; no marked rigidity. In the right hypochondrium was a firm resistant mass, dull on percussion, lying behind the right rectus, and reaching as high as the costal margin. The edge of the liver was not felt. Slight dulness in right flank. Temp. 98·6°, pulse 120.

Having come to the conclusion that his pain was connected with the swelling beneath his liver, and in view of his rapid pulse-rate, unaccompanied by any rise of temperature, I sent him to hospital for early operation, his surroundings making it inadvisable to operate in his small cottage. Cœliotomy was performed on the evening of December 15th under chloroform. The swelling proved to be a distended gall-bladder, which was stitched to the abdominal parietes. After operation he had a fair night, passing flatus *per rectum*, but his cough increased and acute pneumonia developed, of which he died thirty-six hours after operation. The pulse remained rapid, about 120, with respirations 32 to 36, rising shortly before death to 44. The temperature for twenty hours following operation was not above normal, rising just before death to 100°. There was no autopsy.

Comments.—The above case is in many ways similar to those described by Mr. H. L. Barnard in the *Lancet* of August 2nd, 1902. The distended gall-bladder was a herring across the trail, and probably had little to do with his pain. It is a matter for regret that no special attention was directed to his thorax prior to operation, but in a man of seventy-one with a large barrel-shaped chest, the subject of chronic winter cough and emphysema, it is very doubtful whether examination would have revealed more than an ordinary amount of bronchitis. The pulse-rate of 120 was quite consistent with a respiration-rate of 30, while the normal temperature, with pain referred to the region of the abdominal swelling, was equally misleading.

PLYMOUTH.

Of Minor Head Injuries.

A Paper read before the Abernethian Society, November 26th, 1902.

By A. J. FAIRLIE CLARKE, M.B., B.C.

IT is not my wish, Mr. President and gentlemen, to say anything new about either the diagnosis or treatment of minor head injuries, and my only excuse for bringing so commonplace a subject before the Society's notice is the very triteness of that subject. Every one here has seen something of the slighter forms of injury about the scalp and face, and so every one may have a word to say in the discussion which I hope is to follow, either in criticism or confirmation of what I am about to say.

I shall endeavour as far as I can to confine myself to the clinical aspects of my subject, and to trace the course of a patient from his arrival at the hospital to his ultimate discharge therefrom.

By far the larger number of our patients walk either alone or with friendly assistance to the hospital. But we will assume that our patient has been carried unconscious to the surgery. It is then important to find out what is the cause of his unconsciousness.

You are all doubtless aware of the old *memoria technica* for the causes of unconsciousness in a patient found in that state. Taking the vowels of the alphabet we have one cause beginning with each letter. But as an exception we must say that the letter A stands for two conditions producing insensibility. Thus—

A stands for alcohol poisoning and
" " apoplexy.
E " " epilepsy.
I " " injury.
O " " opium poisoning.
U " " uræmia.

To these must be added one or two other states, such as diabetic coma, and the results of some other poisons, as carbolic acid and the like.

Now head injuries, as we have just said, may be the cause of our patient's loss of consciousness; but they may also result from his falling and damaging himself as he became unconscious from some other cause. But it is only of unconsciousness the result of blows on the head or of the injuries themselves that I mean to speak. To include all the other conditions under which a patient may lose himself and injure his head would lead us too far; nor will time allow us to go into the differential diagnosis of these varied states, depending as they do on the past history of the patient, the statements of relations or of persons who saw the injured man lose consciousness, the odour of the breath, the condition of the urine, the size of the pupils, the state of the fundus oculi, the contents of the stomach, and so forth.

We have incidentally mentioned the patient's history, and one of the first things to do when we see the case is, if possible, to obtain some account of the way in which, and the instrument by which, the injury was produced. In this way some idea may be formed of the injuries which might be expected when the physical examination of the patient is begun. For instance, sharp-pointed instruments would be likely to produce punctured wounds and fractures more serious than might at first sight appear to be the case. Again, thin instruments, like foils or umbrella points, have caused serious mischief with but few signs when driven up the nose or between the globe of the eye and the upper eyelid, thus penetrating the thinnest parts of the base of the skull.

Heavy flat or rounded objects striking the scalp are liable to cause fissured fractures of the vault or base of the skull. The same may occur from falls on the feet or buttocks, when the vertebral column is driven forcibly against the occipital condyles.

History may be of value to the surgeon in another way, namely, medico-legally, by directing investigations to the possibility of the injuries being produced in the way described.

We have assumed that our patient has been brought unconscious to the hospital, and we have yet to determine the extent of his injuries. Now this cannot be done in a moment, and it is for this reason that all patients brought under our care suffering from head injuries are detained so as to be under observation for at least an hour. If the patient has been rendered unconscious it is well to detain him longer, say an additional hour for every ten minutes of unconsciousness.

Now, to determine whether an unconscious man is suffering merely from concussion, a state as a rule sooner or later completely recovered from, or from cerebral compression, a state as a rule ending in death, is not a matter which can be settled by a single observation, but rests on the collective evidence of a variety of signs.

In concussion the patient can generally be roused, is nowhere paralysed though he may be generally lax in muscle from shock, has a frequent, small, often irregular pulse; has shallow breathing, has equal active pupils, may involuntarily pass water, and has a surface temperature which, though it may be as low as 96° or 97° F., is uniform on the two sides of the body.

In compression, on the other hand, the patient can generally not be roused, has local paralyses which later become general, has an infrequent, large, and regular pulse; has deep, regular, stertorous breathing; has unequal active pupils until the last stage, when they are both dilated and fixed. He does not pass his water, but when the bladder is full urine dribbles away. The surface temperature, which is frequently raised a degree or two, may be different upon the two sides of the body.

The above signs taken together enable a pretty accurate estimate of the patient's condition to be formed, but they cannot be relied upon if taken singly. For instance, a patient in the first stage of compression may be more easily roused than one who is severely concussed. Again, the pulse, which at first is infrequent and large in compression, later becomes frequent and small like that found in concussion.

The most valuable distinction between the two is, I think, the presence or absence of muscular paralysis. Should the patient have a local palsy the case is almost certainly one of compression, provided of course that it is certain that the palsy did not exist previous to the receipt of the injury.

The rapidity with which compression comes on varies with the nature of the compressing force—immediately from bone, in a few hours from blood, and in a few days from inflammatory processes or spreading œdema.

The cases of compression which are amenable to surgical treatment are—

(1) Those due to depressed fractures.

(2) Those due to extravasation of blood between the bone and dura mater.

These latter may be distinguished from hæmorrhages into the deeper parts of the brain by the paralysis being local, not hemiplegic or general, and by the occasional occurrence of spasmodic movements of groups of muscles whose motor cortical centres lie in the compressed area. Hæmorrhages, too, into the retina are less common in extra-dural than in hæmorrhage into the internal capsule or other deep parts of the brain.

(3) Local compression due to abscesses and the like.

But it is not of compression that I wish to speak, for that is not a sequel of a minor injury, and of the diagnosis of concussion enough has been said. Its treatment will concern us later. The only other point to which I want to refer before we turn to the local condition of the patient's head is vomiting.

Now vomiting, I take it, after concussion is a good sign. One hears it spoken of from time to time as if it were a most serious thing. But as far as my experience goes it is always the beginning of reaction, and with it the pulse improves, and the patient gradually recovers from his condition of shock. This vomiting is most common in children, and is a particularly favourable sign in their case.

We now turn to the local examination of the injured head. The whole head should be examined for bruises and other injuries. Often when there is a very obvious wound on one side of the scalp a graze or wound will be found on the opposite side, where the head has been dragged along the ground. Such a secondary injury might be overlooked.

Most of the local signs of head injuries are due to the escape of blood either into the tissues or externally from a wound.

Of effusions of blood into the tissues the most common is that in which the hæmorrhage takes place into the dense cellular layer of the scalp between the skin and the aponeurosis of the occipito-frontalis. It here gives rise to a more or less tense fluid swelling, through which the uninjured bone can be felt lying beneath it. It is this kind of bruise which sometimes simulates a depressed fracture, for a hard sharp ring may be felt round its margin dropping down abruptly to the smooth bone beneath. But such a ring is due to the clotting and fibrous changes in the blood, and will be found to yield under steady pressure with the finger, thus showing that the condition is not due to a broken bone.

Blood beneath the pericranium would be confined to the area mapped out by sutures. The pericranium is firmly adherent to the bone along the sutures, and blood effused beneath it should be confined to the area of a single bone. This form of hæmorrhage is most common in childbirth.

Blood effusions about the face vary much with their situation, whether the cellular tissue is dense or lax where they occur. Hæmatomata may assume very curious shapes if bound down by the adhesions of old scars, and I have seen such a bruise on the forehead, which suggested at first sight a depressed fracture from a curious pit there was in its edge, but which on closer examination was found to be merely the site of an old scar.

From the looseness of the cellular tissue about the eyelids much blood often escapes into them, causing great swelling and discoloration of the parts,—in fact, the familiar black eye. Such effusions of blood, however, cannot pass backwards into the orbit and subconjunctival tissue on account of the palpebral ligament, which, as you know, passes from the periosteum of the orbital margin to the tarsal cartilages. The same ligament prevents blood passing from behind forwards from the orbit to the lids. Speaking on this subject Erichsen says, "In the ecchymosis from fracture the extravasated blood advances from the orbit, and is shut off from the subcutaneous tissue of the lids by the palpebral ligament, while it readily finds its way beneath the conjunctiva. In the more severe cases the lids may be tense, greatly swollen, and of a bluish-purple colour; the subconjunctival tissue distended with blood, and the eye distinctly protruded. It is only when abundant that subconjunctival hæmorrhage is of any value in the diagnosis of fracture."

Subconjunctival hæmorrhage is always bright red in colour, from the ease with which the hæmoglobin gets oxygen through the membrane from the outer air. Most subconjunctival hæmorrhages are due to rupture of conjunctival vessels, and have their greatest extent in front near the corneal margin. Such hæmorrhages may be distinguished from blood coming from the back of the orbit by this fact. Should the blood come from behind, when the patient looks up the staining will become deeper the further back we can see, instead of fading gradually away as a local hæmorrhage would do.

Bleeding from wounds of the scalp and face is generally free, and is more free from incised than from lacerated wounds. Some of the freest bleeding from a scalp wound that I have seen came from a small incised wound only an inch long, which an Italian, living on Saffron Hill, had received from a playful rap his wife had given him with the carving knife. This free bleeding is due to the dense cellular tissue in which the vessels of the scalp run, and which prevents the proper contraction and retraction of the cut artery. Sometimes, too, a vessel is but half cut across, and what contraction does occur only tends to make the edges gape still more.

Bleeding from the nose is common in head injuries, and is usually produced by some direct injury to the face. Frequently it is of little importance, but it may if persistent be serious.

Bleeding from the ears is less common, and more apt to be of serious import. It may be due merely to slight injuries about the external meatus, or to laceration of the membrana tympani, as occurs in artillerymen from the detonation of their guns. But bleeding from one or both ears is always suggestive of a fracture extending through the petrous portion of the temporal bone, and such fractures are, as a rule, not confined to that bone, but extend widely across the base of the skull. But it is not the bleeding so much as its persistence which is diagnostic of fractured base. Superficial hæmorrhage soon stops, but the oozing from a broken bone continues for hours, and may then gradually change from blood to cerebro-spinal fluid. This long-continued oozing from nose, ears, or mouth is almost pathognomonic of fractured base.

Bleeding from the mouth, too, may be due to slight causes, as a bitten tongue or injury from a pipe-stem. But long-continued oozing, blood trickling down the back of the pharynx, or the vomiting from time to time of quantities of swallowed blood are all suggestive of injury to the base of the skull, though they all do occur in simple nose bleeding. Again, it is on the continuance of the bleeding that stress must be laid.

The examination of the wound is so intimately connected with its dressing that I will not specially mention that until I come to the subject of treatment. But before beginning this there are still a few phenomena which may be met with in the examination of the head.

One of these is surgical emphysema. You know that in whooping-cough some air vesicle may give way, the air escaping into the cellular tissue of the mediastinum. With prolonged coughing the air is driven upwards into the neck, and in time extends over the whole body, giving rise to the peculiar crackling sensation which we associate with surgical emphysema. Again, in tracheotomy wounds air may escape into the cellular planes of the neck, and so reach the head. The same thing may occur in cut throat or other wounds of the air-passages if they are completely sewn up, and for this reason such wounds should never, as a rule, be completely closed, but a drainage-tube or other means of escape be left for any air which might escape into the tissues.

But it is not to such emphysema reaching the head from other parts that I would refer. Air may be extravasated after injury to any of the air-containing cavities of the face, the frontal or ethmoidal sinuses, or the antrum of Highmore. Most frequently it is from the anterior ethmoidal cells that the air comes, the thin lachrymal bone having been broken by direct injury.

I remember when doing, I think, my first night duty as a dresser in the surgery such a case as this. A robust man had, shortly before I saw him, received a blow in his left eye from a stiff stable brush, and had considerable swelling of the lids of his left eye. The swelling had the characteristic feel of surgical emphysema, and was obviously mainly composed of air. On asking the patient to blow his nose, which he did with vigour, the whole eyelids swelled to double their former size, thus showing the communication between the swelling and the nasal fossæ. For the guidance of future dressers I would add that the house surgeon was not much pleased with the experimental pathology I had carried on in his absence. At the time this swelling was thought to be due to a fracture extending into the frontal sinuses, though I do not think there was any direct evidence of such an injury. The condition might quite as probably have been due to a broken lachrymal bone, which is, as we have seen, its commonest cause. I can hardly imagine a brush breaking so strong a bone as the frontal, for it was with the bristles that the man was struck.

During my last period of duty I have seen another similar and most instructive case.

A man had the previous evening been set upon by a gang of roughs, and had his face somewhat severely handled. His left eyelids were a little swollen and bruised, and on the outer side of

his left eye was a bright red subconjunctival hæmorrhage with its maximum intensity near the corneal limbus, but fading gradually and completely away as it was traced backwards.

His right eyelids were considerably ecchymosed, swollen, and when felt gave evidence of surgical emphysema. On forced expiration with the mouth and nose closed this swelling of the eyelids was increased. There was also extensive subconjunctival hæmorrhage of the lower half of his right eye, extending as far back as could be seen. What must, I take it, have happened was that one of the blows the patient received in his right eye broke either his lachrymal bone or the orbital plate of the ethmoid. The bleeding from this had gravitated to the floor of the orbit, and had extended forwards, stripping up both ocular and palpebral conjunctiva as it went. At the same time air escaped into the cellular tissue of the lids. It was interesting to see surgical emphysema and the two varieties of subconjunctival hæmorrhage in the same patient.

Injuries of the cranial bones seldom come within the category of minor head injuries. It is true that simple fissured fracture of the vault may be passed over as a minor head injury, for I know of no sign other than subpericranial hæmorrhage to point to it. But most fractures of the cranial bones, if they can be diagnosed, are serious, for then they are either compound or depressed.

Yet fractures of the facial bones are not infrequent, and the two sides of the patient's face should be compared with this in view in cases where such injuries are suggested by the nature of the accident. A finger in the mouth will often be of service in such an examination.

The soft cranial bones of children may be dinted inwards without fracture, a spoon-shaped depression being produced. Such cases should be kept under observation, but as a rule the bone either regains its normal contour by its own elasticity, or, though the deformity remains, no ill effects follow.

Before we go on to the subject of treatment there is one precaution to be observed which I would mention, namely, to examine the patient for injuries other than those of his head, and not to send a patient into a ward, as has been done, with an undiagnosed fracture of the humerus as well as a cut head.

Once again, head injuries may be the sequel of other trouble, which you may overlook. One morning a small girl was brought to the surgery with the history that she had on the previous day fallen and bruised her forehead. She seemed a little seedy, but not more so, I thought, than might have followed some slight concussion; but next morning she presented a well-marked smallpox eruption, and the fall must have occurred during the prodromal stage of the disease.

Shortly afterwards a small boy was brought up with the same history, that he had fallen on the previous day and hurt his head, and there was a distinct bruise on his forehead to confirm this story. But he looked too ill for this to account for all his trouble, and I suspected that this boy was going in for an acute fever. Such was indeed the case, for next day the boy had a bright scarlet rash, but unfortunately he died suddenly before the ambulance arrived to take him to the fever hospital.

The treatment of any head injury falls naturally into two divisions: first, the treatment of the patient; and secondly, the dressing of his local mischief.

If, as we have assumed, our patient is unconscious, suffering from concussion when first seen, our aim should be to treat the condition of shock associated with the first stage of that concussion. He should be kept warm, and not exposed to cold more than can be avoided during the necessary examination, but wrapped in blankets; and if the collapse is great, hot bottles at the feet may be of service. Excessive draughts of cold air, such as are now and then found in the back room of our surgery, should be avoided. At this stage the head should be kept low. No stimulant should be given unless urgently called for by the state of the pulse. By this time our patient is probably conscious, and soon the stage of reaction begins, ushered in, as we have seen is so frequently the case, by vomiting. Now the head may be slightly raised, and the patient kept as quiet as possible in the recumbent position. If the man is in bed cold may now be applied to the head, either by means of an ice-bag or Leiter's tubes. Most patients whom we see in the surgery here, however, are left to lie for a while on the couch in the back room until sufficiently recovered to be taken home. But before he goes he should be given a purge to clear his bowels well out, and so lower his blood-pressure. Nothing is found practically to be of more value than this in the treatment of head injuries, whatever its explanation may be. The best purge to give is calomel, and my own practice has been to order gr. v to be taken either at once or when the patient reaches home. For children a somewhat smaller dose should be given.

In Mr. Langton's wards it has recently been the custom to give gr. x of calomel to patients with head injuries, and no doubt this is a good plan. But it is a matter on which authorities differ as to whether gr. x are more effectual than gr. v, especially when followed up next morning by a saline purge such as ℥iss of house physic. For out-patients I prefer the smaller dose.

As to seeing our patient again, the best plan, unless for some special reason we wish to see him sooner, is to advise him to go home and go to bed, to stay quietly at home next day, and to present himself for re-examination on the third day. As a rule it is needless to see the patient on the day following the accident, and he would be better advised to remain quietly at home, and to partake merely of a slop diet.

Of the treatment of the head injuries themselves we will consider first bruises.

Hæmatomata of the hairy scalp usually require no local treatment, but get well without your interference. If, however, you wish for form's sake to do something, either bathing the part with cold water or the application of gentle pressure with a bandage may be recommended as innocuous methods of treatment.

Should the hæmatoma, however, instead of being gradually absorbed, suppurate, as they sometimes will, a week or ten days after the accident, it should be treated as an ordinary abscess, by incision and drainage.

Bruises about the face and forehead may be treated either by the application of heat or cold. A hot fomentation, I think, relieves pain more than the application of cold by means of an evaporating lotion, and children, I fancy, prefer the hot application. But there is no objection that I know to the use of, say, lead lotion to bruises about the face, provided that the eye itself is not injured. If the corneal epithelium has been injured lead lotions should be avoided, as being liable to form opacities in the cornea. But apart from such injuries, lead lotion may be as safely used about the face as elsewhere.

With wounds the first thing is the temporary arrest of bleeding, and this can generally be done by the application of firm pressure with a pad of gauze over the bleeding point. With this pad pressed firmly over the wound the hair should be cut freely round the wound, and then the scalp shaved, the edges of the wound being shaved last. For this to be done the pad must be removed and bleeding controlled by digital pressure if necessary.

The shaved area should have, I think, a radius of not less than one and a quarter inches on all sides of the wound, and the hair should be so cut that no long locks are left which might draggle over the wound. If the wounds are extensive the whole head should be shaved.

The scalp after shaving should be cleansed first with soap and water, next with turpentine, and finally with some antiseptic solution such as 1 in 2000 perchloride.

The wound can now be examined by inspection and afterwards by palpation. When as much as can be has been seen, a clean finger should be introduced into the wound if it be large enough, and the injured parts carefully felt; in this way much more can be learnt than is possible with a probe. Depressions or fissures in the bones can be best made out in this way, and the latter distinguished from a sharp edge of periosteum. If, however, the wound will not admit the finger it should be carefully examined with a clean probe.

Surgeons differ as to the amount of cleaning which a scalp wound requires. Any shreds of badly crushed scalp should first be removed, but so great is the reparative power of the tissues that scalp flaps very rarely slough.

The wound should be well washed with soap and water. If much mud has been ground in too vigorous scrubbing with a nail brush is to be avoided, as liable to do more harm by direct injury to the tissues than good by the removal of dirt. Wounds heal readily, although all the mud may not have been removed, and I have seen a case in which dirt was ground into a groove in the bone produced by a cart-wheel heal rapidly without misadventure. Still, as much dirt should be washed away as may be without undue violence.

Turpentine may next be swabbed over the wound to remove any fat and grease, after which a thorough washing, and if there is any pocketing of flaps, syringing with an antiseptic lotion should follow.

If by this time the bleeding has not ceased it should be stopped. Now pressure forceps and ligatures are of little use in scalp wounds. I have seen four or five pairs of pressure forceps on a scalp wound without checking bleeding, which was soon controlled by the pressure of a graduated compress. The best means of arresting bleeding

from the scalp are sutures and pressure. If a suture be passed deeply through the scalp just beyond the bleeding vessel and then drawn tight the hæmorrhage will cease at once. Little harm will come of this method of arrest even in large wounds, provided that free drainage be possible by means of a tube.

In some wounds a graduated compress formed of a series of gauze pads placed one above the other, and kept in place by a firm bandage, may answer better.

Mr. Percy Dean, writing in Treves' *System of Surgery*, says that "no wound of the scalp, unless inflicted under aseptic conditions, should be tightly sewn up without a provision for drainage. This is, in my opinion, a most valuable maxim; and although drainage is important in all scalp wounds, it is especially so when the aponeurosis has been cut and the loose cellular layer in which pus so readily tracks has been exposed.

Dr. Champneys, in his midwifery lectures, used to, and I dare say still does draw attention to the importance of drainage by recalling the fact that it was through dry places that the unclean spirit walked, seeking rest and finding none. Similarly, pyogenic organisms have much less chance of multiplying in it if a wound be kept dry; but, on the other hand, grow rapidly in moist dead matter, such as the exudate from a wound, and so give rise to sapræmia and perhaps septicæmia.

Drainage of large wounds is carried out by means of rubber tubing, while in smaller wounds gauze plugging (badly so called, for it should not be used as a plug or cork, but merely to keep the wound open and allow the exudate to escape beside it, and not be pent up within) may be used. In small wounds a thin roll of gutta-percha tissue will often make a very efficient drain.

Such drainage will require to be continued for a week or ten days in large wounds, but in small wounds the gauze should be removed after twenty-four or forty-eight hours. There is one disadvantage in draining small wounds in our hospital work here, namely, that if the night dresser on Saturday puts a gauze plug in a cut head, the day dresser, busy with a Monday morning duty in the surgery, merely asks if the head is comfortable, and hearing that it is, tells the patient to return on Thursday without disturbing the primary dressing. The drain thus remains in place for six days, which is undesirable. A note on the patient's paper stating that drainage was being employed would prevent this.

Drainage being provided for, the wound must be closed. In some wounds of a flap nature which have not reached the aponeurosis the edges fall into place without stitches, and such cuts may be kept closed merely by a dressing and bandage. Starred and other jagged wounds are often best left unstitched. But edges which gape must be brought together by suture. Those wounds gape most in which the aponeurosis of the occipito-frontalis has been divided, and of these transverse wounds on the brow or occiput and vertical wounds in the temporal region gape most, as you would expect.

Torn flaps of scalp should be gently drawn back into position and fixed there with stitches. Salmon gut is the best suture material for the larger scalp wounds, though horsehair does well enough for smaller cuts. Stitches in the scalp should be removed after a week unless there is great tension upon them, when they may be left a day or two longer.

Wounds about the face are of such importance from the æsthetic point of view that they must receive more than ordinary care. As a general rule we may say that all cuts on the face require to be sewn up. As exceptions to this may be mentioned some superficial wounds about the eyebrows and lids, where the cut running in the direction of the skin folds will leave little noticeable scarring when it has healed.

Very fine sutures should alone be used on the face. Horsehair is undoubtedly the best material. Should there be so much tension on the flaps that horsehair is not strong enough to keep the edges in place, then salmon gut must be used, and there will be so much scarring from the severity of the wound that a few stitch marks will not be of much consequence.

Sutures of whatever kind should be removed early from the face, that is on the third or fourth day, for if left in longer they are liable to leave permanent scars. If at this time the wound shows a tendency to gape the edges may be drawn together by strips of strapping. A familiar example of this method is seen in the use of strapping after operations for harelip.

Cuts about the lips require careful suturing to ensure the red margins being in line; while tags of mucous membrane, torn from the inner aspect of the lips or cheeks, may either be snipped away with scissors or fastened in place with a point or two of horsehair.

Wounds of the tongue, produced as they so generally are by the patient's own teeth, should be sewn up, the sutures being passed deeply so as to prevent any pocketing, in which septic material from the mouth might be retained.

In all cases of wounds extending into the mouth the patient should be given a mouth wash, with which he is to rinse his mouth frequently. There are many good washes for the purpose, as the Gargarisma Aluminis Composita of the H.P., Lotio Acidi Carbolici cum Iodo, formalin 1 in 500; but perhaps nothing answers better and is pleasanter to use than Sanitas diluted with water. The strength used may be anything between ʒij to Oj, and equal parts of the two.

The object of putting a dressing over a wound is twofold:

(1) To absorb any discharge there may be, and drying this up, leave no suitable soil for micro-organisms to grow upon.

(2) To prevent any organisms from reaching the wound from without.

These two objects are gained by the use of any sterile absorbent material, and the second made more certain by that material being impregnated with an antiseptic. Head wounds are usually dressed with several layers of such medicated gauze.

Sometimes dry iodoform powder is sprinkled over the wound, but personally I prefer not to do this, as I think it is apt to cake and cause retention of discharges, and—a minor point—it obscures the stitches and makes them more difficult to remove. In some indolent and sloughing sores, however, I think it is of use in cleaning the wound and promoting healing.

The ordinary collodion dressing is not a good one for the scalp when the patient is first seen, and should not, I think, be used about the face unless the gauze cannot be kept in place by a bandage or strapping. Later on, when the stitches have been removed and there is no discharge to be pent up, collodion forms a most convenient covering for any wound.

Primary dressings are best kept in place by some form of bandage, but strapping can be used for wounds about the face and neck. But where the parts are covered with hair strapping cannot be made to adhere.

For most wounds some variety of the figure-of-eight bandage is generally used, but it is always a mystery to me why the triangular bandage is not more used in out-patient work. True, for a dressing which requires firm pressure it is not suitable, yet how often we wish to apply fomentations to the head! and what is more convenient than a triangular bandage when the patient is required to change it frequently for himself? Various other modifications of the scarf bandage should be of use in special cases.

The Capelline bandage is too hot and heavy for constant wear, however fascinating it may be to put on, and unless very well applied it is liable to come off bodily. A more comfortable bandage for wounds on the top of the head is made by taking a turn of bandage over the vertex, bringing it down in front of the right ear under the chin, round the back of the neck, and up again behind the right ear, and so to the vertex, when the same procedure is repeated, only substituting left for right. This is a most secure form of bandage, and cannot slip off as the Capelline may.

The eye bandage is a most useful one for wounds of the upper part of the face, while the jaw bandage is convenient for cuts about the chin.

Our patient is now dressed, and, after taking the purgative medicine we have prescribed, should be able to get home.

The after treatment of his wound requires little mention, provided it pursues a favourable course, as it probably will do if well drained from the first. But should the case not have been seen from the outset, wounds may require opening up, pockets of pus freely laying open, tubes inserted, and fomentations applied.

Should a wound suppurate after our treatment has been carried out from the start, the same line must be followed of free drainage and warm moist applications. Sloughs formed from the tough tissues of the scalp are very slow to separate, and should they form this line of treatment will have to be pursued for a considerable time.

Some patients suffer for a longer or shorter time after their accident from headache, and the best treatment I know for this condition is to ensure regular action of the bowels and to give small doses of bromides. The Haustus Gentianæ c̄ Potassii Bromido given three times a day generally meets the case exactly.

There is not much I wish to say of the complications of head injuries. In old folk any injury is liable to be followed by lung trouble if the patient is obliged to lie abed for any length of time, so I should advise that any such patient be got up in a chair as soon as may be. That this is no fancy danger is evidenced by the case of

an old man who was admitted into Coborn Ward last summer suffering from a neglected scalp wound; for though the wound was cleaning nicely the patient developed bronchitis, of which he died some three weeks after his admission to the hospital.

In conclusion, sir, I feel that much has been left out which might have been mentioned on this important subject. Time has not allowed me to speak of the anatomy or pathology of scalp wounds and the like, and I must apologise for the disjointed way in which the remarks I have made have been strung together. I hope, however, that what has been said may be sufficient to excite some discussion upon minor head injuries, their diagnosis and treatment.

St. Bartholomew's Hospital Amateur Dramatic Club.

THE twentieth year of the Hospital Dramatic Club was signalised by the presentation of "A Pair of Spectacles," on the nights of January 8th and 9th. The performance took place as usual in the Great Hall, and the audiences were both large and appreciative.

One or two changes in the customary order of things deserve notice. The bill was a single one, and this seemed an advantage; for except in the case of a few good dialogues it is difficult to find short pieces that are deserving of careful study and acting. And as the acting always improves as a piece progresses, it follows that it is generally unwise to multiply beginnings. Then, again, a single bill prevents the loitering of the audience during a long interval, yet allows of the entertainment of visitors by the resident staff at the close of the piece if it is not too long. The late rise of the curtain—7.45 instead of 7—is another improvement, allowing dinner to many of the audience before coming. We should suggest one other thing for future performances,—that refreshments be postponed until after the piece is over. If this were done the curtain need not rise till 8, and dinner would then be practicable to most.

The choice of Grundy's masterpiece was bold, seeing that the majority of the audience must have witnessed the Garrick performance by Mr. John Hare's company. But, as is often the case, this boldness was rewarded, and we are glad to say that it did not in any way depreciate the standard of the performance.

"A PAIR OF SPECTACLES."

A Comedy in Three Acts,

By SYDNEY GRUNDY.

Mr. Benjamin Goldfinch	Mr. R. J. WAUGH.
Uncle Gregory (his Brother)	Mr. K. D. BELL.
Percy (his Son)	Mr. S. E. CRAWFORD.
Dick (his Nephew)	Mr. R. C. P. BERRYMAN.
Lorimer (his Friend)	Mr. P. A. LLOYD-JONES.
Bartholomew (his Shoemaker)	Mr. P. BLACK.
Joyce (his Butler)	Mr. A. J. KENDREW.
Another Shoemaker	Mr. P. A. LLOYD-JONES.
Mrs. Goldfinch (his Wife)	Mr. A. H. MUIRHEAD.
Lucy Lorimer (Lorimer's Daughter)	Mr. P. O'BRIEN.
Charlotte (a Parlourmaid)	Mr. F. RICE.

ACT I.—*A Breakfast Room in Mr. Goldfinch's House.*
ACT II.—*The Same—next Morning.*
ACT III.—*The Same—Evening.*

Stage Manager—Mr. R. C. P. BERRYMAN.
Assistant Stage Manager—Mr. P. A. LLOYD-JONES.
Acting Manager—Mr. K. D. BELL.

The parts of the two brothers Goldfinch were admirably played by Waugh and Bell. Waugh, as the benevolent Benjamin, was perhaps a little too violent at times, illustrating the cumulative effect of emotional acting, always difficult to avoid. And we might add that an introductory and half-unconscious "ah!" sometimes spoiled the crispness of a smart repartee. But the acting was, apart from these small points, quite good, and the changed outlook upon life, with its reacting effects upon Goldfinch's mind, was well portrayed.

For the Gregory of Bell we have nothing but praise; neither the brusqueness nor the brogue of the Sheffield skinflint was overdone, which argued considerable forbearance, and all the possible points in this admirable character were fully made.

Berryman, as nephew Dick, was also a great success, and fully justified his being cast for this rather than for one of the female parts, in which we remember him to have done exceedingly well on previous occasions. We would like to hint, however, that the favourite shrugging gesture indulged in by this actor was not always well adapted to the emotion it accompanied. Fortunately the state of Dick's fortunes does not call for much action of any sort.

Crawford, as Goldfinch's son Percy, was the easy, composed, and comfortable young fellow he should be, yet scarcely showed enough life when he came to a puzzled attempt at explaining his father's change of character. Here we felt that Percy knew too much about the *motif* of things to act his part as it deserved, which surely is that of surprise and mystery, shared by his mother, who also, by the way, rather failed to give expression to these feelings.

Lloyd-Jones, in the part of Lorimer, seemed to us a little too tragic. His voice falls to a tone suggestive of great despair at the end of most sentences, and this, too, when the *Morning Star* is sighted as well as when she is overdue. But his "get-up" was quite good. In taking the part of the second shoemaker the same actor was seen to better advantage. Black, as Bartholomew, played a small part very well, and gives good promise for the future. Kendrew, as Joyce, gives even greater promise, and we shall look forward to his being cast for something larger next year.

Of course the impersonation of women by men can never, in the nature of things, be without its humorous side; there are anatomical differences which cannot be overcome, and physiological ones in voice and gait which elude the best efforts at elimination. A square chin, a

broad chest, and a vocal compass which is an octave lower than the average female's, are things which nature insists upon as masculine attributes, and they compel a smile from necessity. A clap on the back, however gentle, or the failure to return a rather large handkerchief into a very small pocket after several attempts, is apt to complete the picture on the comic side. But these difficulties were nearly as well met as they could be, and we are not ignorant of the fact that no inconsiderable part of the audience's interest turns upon these efforts. Muirhead, as Mrs. Goldfinch, is to be congratulated upon his mastery of a part taken at very short notice. It was a little unfortunate that O'Brien was cast for a part which did not suit him. His Lucy Lorimer, however, was again, we gather, undertaken to help the Club out of a difficulty. We can picture his talents displayed to better effect in a male part. Rice, as the maid Charlotte, succeeded in managing a most effective "get-up."

The scenic effects were admirable throughout, leaving nothing to be suggested. Yet on inquiry we find that this was due to their rearrangement at the last moment by the members themselves. Perhaps it is a hypercriticism to wish that they had added to their already extra work the oiling of the curtain.

The stage management deserves hearty congratulation, and was in all points beyond criticism.

The overture and incidental music were supplied by the Hospital Orchestral Society, under the direction of Mr. A. F. Forster, with Mr. A. A. Hamilton as leader. The following were the items played during the evening:

MUSIC PROGRAMME.

1. OVERTURE . .	William Tell . .	*Rossini.*
2. VALSE . .	Estudiantina . .	*Waldteufel.*
3. SELECTION .	Toreador . .	*Godfrey*
4. SYMPHONY II		*Haydn.*

Musical Director—Mr. A. F. FORSTER.
Leader—Mr. A. A. HAMILTON.

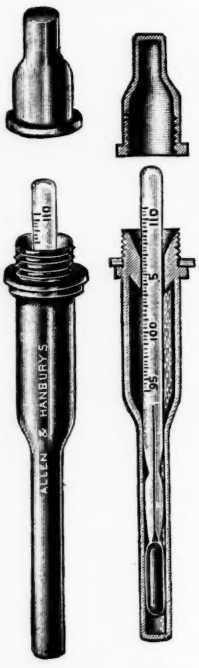
A full orchestra was present, and the rendering of the music was better than we ever remember it. Mr. Forster seems a born conductor, and his management of his orchestra was admirable. History says that there have been times during the long ago when the stage manager was driven to send a message to the conductor threatening future boycott if he did not forthwith cease playing. The times have changed.

The Bart.'s Dramatic Club can now count its age in decades, and is the oldest, or very nearly the oldest, of its kind in London. Writing as a non-member, it is obvious that its reputation is fully deserving of the attention of men coming up to the Hospital; and however good a man may be, he need scarcely fear that he will be wasted by joining it. Anyone possessing histrionic tendencies should throw in his lot with it. We learn that the subscription is 5*s.* a year, and that the Club at present counts about twenty available members.

We understand that the Club is much indebted to past members, specially to Messrs. Emlyn, Townesend, and Valerie, for its continued prosperity until now. We referred to this as the twentieth performance, which reminds us that it will next year reach its majority. May we not only be able to congratulate it upon this event, but see it safely launched upon the full tide of a successful adult life.

New Appliances.

DR. RICHARD THORNE THORNE (Woking) writes: I am taking the liberty of drawing your attention to an antiseptic clinical thermometer case designed by me. Realising the danger of using a septic clinical thermometer, and the absolute impossibility of keeping it aseptic by the ordinary methods of washing it in cold water after use, I had the case (shown in the illustration) made, and having used it now for more than a year I have found it efficient and convenient. The essential principles of the case are, first, its being watertight; and secondly, its capability of holding a sufficient quantity of antiseptic solution in moderate compass. The first condition is effected by having an india-rubber washer on the flange, and the second by having the middle half of the case of a larger diameter than the upper and lower portions. When in use the case is filled two thirds full of carbolic solution of whatever strength desired—I usually employ 1 in 10. The result of inserting the thermometer is that the level of the solution rises so as nearly to fill the case. When the thermometer is in use the case can be laid on any flat surface without leakage, on account of the cone flange at its mouth (shown in illustration) preventing the liquid from flowing out. The greatest external transverse diameter of the case is no greater than that of an ordinary gentleman's gold watch, and hence can be carried in the waistcoat pocket without inconvenience. The case is nickel-plated, and neatly made by Messrs. Allen and Hanburys.



Notes.

AT a Court of Governors, held on Thursday, December 18th, Dr. Norman Moore was elected full physician, and Mr. Bruce Clark full surgeon, to the Hospital.

* * *

IN connection with the election of a physician to the Hospital it is interesting to note that the Royal College of Physicians has the right of nominating two candidates. On this occasion the College nominated Sir Wm. Church and Dr. Liveing, its President and its Registrar.

* * *

THE recent examinations at London University have brought two more Gold Medals to Bart.'s men. The M.D. Gold Medal and first place fell to Dr. W. T. Rowe, and the B.S. Gold Medal and first place to Mr. S. R. Scott.

* * *

THERE was an exceptionally large attendance of fifty-four at the Annual Dinner of the Medical and Teaching Staff, held at the Albion Tavern on December 18th. Dr. Claye Shaw, the senior lecturer at Bart.'s, occupied the chair. A traditional toast of the evening is that of the members of the staff who have been appointed to their posts during the past year. This toast was proposed by Dr. Gee, and replied to by Mr. Austin (Assistant Dental Surgeon), Mr. Williamson (Midwifery Tutor), Dr. Riviere (Casualty Physician), Mr. Rose (Assistant Demonstrator of Pathology), and Mr. Thomas (Assistant Demonstrator of Physiology).

* * *

SCENE—Out-patient Room. *Physician* (unravelling the finer points of the case).—"Are you depressed in spirits?" *Patient.*—"Yes, sir." *Physician.*—"Why is that?" *Patient.*—"Well, sir, since I've been out o' work I haven't been able to buy 'em."

Reviews.

PRACTICAL PHYSIOLOGY. By A. P. BEDDARD, LEONARD HILL, J. S. EDKINS, J. J. R. MACLEOD, and M. S. PEMBREY. (London: Edwin Arnold. Price 15s. net.)

The exigencies of time compel the medical student to pass over certain aspects of physiology in order that he may lay greater stress on those portions of the subject which bear most directly on his clinical work; and while it is essential that the student should be thoroughly familiar with the details of the circulation, digestion, and the urine, he can afford to touch but lightly on cell physiology and on electro-physiology. It is with this principle in view that the present volume has been written.

The work under consideration is the joint production of representatives of the physiological teaching staff of three of the largest London hospitals, so that the authors are necessarily in very close touch with the needs of medical students; moreover the authors expressly state that the book is written primarily for such students, and we may say at once that this work is in our opinion one of the best text-books of practical physiology which we have seen.

The book consists of four parts, namely, elementary and advanced chemical physiology, and elementary and advanced experimental physiology. In the experimental sections the authors wisely limit the amount of "drum" work, and lay increased emphasis on the study of the special senses and the vascular system. Chemistry is dealt with very fully in both the elementary and the advanced sections. The chapters on the urine are excellent, as also is the description of the spectroscopic characters of hæmoglobin and its derivatives. We were glad to notice that Kjeldahl's method is fully described as a demonstration in the elementary chemical section.

In the advanced experimental section a large number of experiments are described in illustration of the psychological relations of vision; and the subject of vision, as a whole, is admirably treated.

The illustrations, which are numerous, are extremely good, those of the crystals being perhaps the most valuable. The only detail, and that a trivial one, to which we take exception is the use of Am_2SO_4 as the formula for ammonium sulphate.

In conclusion, we can say without hesitation that the authors of this work have made a very valuable contribution to the literature of practical physiology, and we can thoroughly recommend it to those who are working either for purely medical examination, or for more definitely scientific examinations such as the B.Sc.

THE INTERNATIONAL TEXT-BOOK OF SURGERY. By British and American authors. Edited by A. PEARCE GOULD, Surgeon to the Middlesex Hospital, and J. COLLINS WARREN, Professor of Surgery in the Harvard Medical School. (W. B. Saunders and Co.)

It is with considerable diffidence that the reviewer commences to write an account of such a wide and comprehensive work as the above.

The book has been written by some fifty-five different British and American authors, each contributing an article on the subject to which he has devoted special attention. The result is that the book deals with all the details and branches of surgery in a way that could not be obtained otherwise.

The work has been carefully edited, so as to secure as far as possible a uniformity of standard.

At first sight it strikes one as being very American, and one has to get used to what appear to us strange methods of spelling.

In order to economise space, the authors have, as far as possible, confined themselves to the present recognised methods of treatment, and have omitted antiquated and obsolete forms—a thing which is very commendable. The book is thoroughly up to date, and contains an excellent preliminary article by Professor Ernst on "Surgical Bacteriology." Cabot supplies an article on the "Surgical Pathology of the Blood."

One of the best chapters, in our opinion, in the book is one by McBurney on the "Technic of Aseptic Surgery." The author has here given a very careful and concise *résumé* of the various methods of sterilisation and disinfection, their relative values, and how they can best be applied in order to attain the high level of asepsis which is necessary at the present day.

As is to be expected in such a large book, some sections are not as good as others. It is rather a surprise, however, to note the somewhat scant attention that is given to diseases of the lymphatic glands. Lymphadenoma, for instance, a disease which is at present exciting considerable attention, is dismissed in a few lines, very little reference being made to its symptoms or pathology.

The book is not intended so much for a student preparing for an examination, but rather as a reference book. As such it must prove of very great value, and we have no hesitation in thoroughly recommending it. There is, however, one rather serious drawback: there is only a very scant bibliography. A good bibliography would not materially increase the size, and would greatly add to the value of the work.

The Rahere Lodge, No. 2546.

A MEETING of the Rahere Lodge, No. 2546, was held at Frascati's Restaurant, Oxford Street, W., on Tuesday, January 13th, W. Bro. G. H. R. Holden, M.D., W.M., being in the chair. Bro. Ogle was raised to the degree of Master Mason, and Bro. Dale Wood was passed to the second degree. Grants of five pounds to a Brother in distress and ten guineas to the Royal Masonic Benevolent Institution were confirmed. It was decided to postpone any decision in regard to the formation of the William Harvey Chapter until the next meeting of the Lodge. The Brethren subsequently dined together.

Examinations.

UNIVERSITY OF CAMBRIDGE.

Medicine, Surgery, and Midwifery.—H. W. Atkinson, E. A. A. Beck, H. H. Dale, J. F. H. Dally, G. G. Ellett, R. B. Etherington Smith, H. U. Gould, C. H. Gregory, A. W. Izard, H. D. Ledward, L. Noon, J. E. Payne, R. M. Ranking, H. Statham.

Pharmacology and General Pathology.—H. M. Aviss, W. B. Crowfoot, C. R. Crowther, C. W. Cunnington, H. S. Dickson, T. J. Faulder, F. M. Gardner-Medwin, G. S. Haynes, F. A. Hepworth, G. Holroyd, J. B. Irving, H. F. Marris, R. F. Moore, W. V. Naish, L. Noon, J. G. Slade, E. K. Williams.

UNIVERSITY OF LONDON.

M.D. Examination.

W. T. Rowe (Gold Medal), A. Eastwood, P. W. Rowland, L. A. Walker, W. W. Kennedy (State Medicine).

B.S. Examination.

Pass List—1st Division.—S. R. Scott. *2nd Division.*—H. Burrows, R. C. Elmslie, E. L. Martin.

Honours List.—S. R. Scott, First-class Honours and Gold Medal.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.

The following have been admitted Fellows of the College:—H. W. Pilgrim, V. T. Greenyer, S. R. Scott, F. H. Wessels, H. B. Bailey.

Appointments.

BROWN, C. R. V., M.R.C.S., L.R.C.P., appointed Senior House Physician to the Great Northern Hospital, Holloway.

* * *

CLARKE, HUNTLEY, M.R.C.S., L.R.C.P., appointed Honorary Medical Officer to the Royal Cornwall Infirmary, Truro.

* * *

ELLETT, G. G., B.A.(Cantab.), M.R.C.S., L.R.C.P., appointed Surgeon to ss. "Fort Salisbury."

* * *

NIXON, J. A., B.A., M.B., B.C.(Cantab.), appointed House Physician and Senior Resident Officer at the Bristol Royal Infirmary.

* * *

PRITCHARD, H., M.R.C.S., L.R.C.P., appointed House Physician to Addenbrooke's Hospital, Cambridge.

* * *

ROBINSON, C. C., M.R.C.S., L.R.C.P., appointed second Assistant Medical Officer to the Manor Asylum, Epsom.

* * *

TURNER, C. H., M.R.C.S., L.R.C.P., appointed Senior House Surgeon to the Royal Infirmary, Halifax.

* * *

WOODWARK, C. S., M.R.C.S., L.R.C.P., appointed Assistant House Surgeon to the Royal Infirmary, Halifax.

New Addresses.

AMSDEN, W., Chalford, Gloucestershire.

CALVERT, JAMES, 113, Harley Street, W.

CHOLMELEY, M. A., 46, Lemon Street, Truro.

HARMER, W. D., The Warden's House, St. Bartholomew's Hospital, E.C.

HARRIS, H. G., St. John's, Birchington-on-Sea.

SODEN, W. N., Upcote, Mapesbury Road, Brondesbury Road, N.W.

STOWELL, T., Melrose, Preston Park, Brighton.

WHITAKER, L. E., The Cottage, Diss, Norfolk.

WORTHINGTON, G. V., Newent, Gloucestershire.

Birth.

ADDISON.—On Sunday, December 21st, at Wican Croft, Northwood, Middlesex, the wife of Christopher Addison, M.D., F.R.C.S., of a daughter.

Marriages.

MATTHEWS—JOHNSTON.—On September 30th, 1902, at St. Mark's Church, Surbiton, by the Rev. R. B. Rankin, M.A., Rector of All Saints, Newtown-Cunningham, assisted by Ven. Archdeacon of Raphoe and the Ven. Archdeacon of Kingston-on-Thames, Ernest A. Churchward Matthews, M.A., M.B., etc., Cantab., Lieutenant I.M.S., only son of Daniel Matthews, Esq., late of Penarth, Glam., to Anna Stewart, only daughter of Robert Johnston, Esq., of Hillside, Parkland, Surbiton.

CARTER—WOOD.—On December 3rd, 1902, at Paisley, by the Rev. W. M. Metcalfe, D.D., Frederick John Carter, M.R.C.S., L.R.C.P., of Sea View, Isle of Wight (son of the late Rev. Canon Carter, of Linton, Kent), to Janet Lang, eldest daughter of John A. Wood, Esq., of Parkgate, Paisley, N.B.